

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing

(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION

See paragraph 2 below

International application No.
PCT/EP2004/003055

International filing date (day/month/year)
23.03.2004

Priority date (day/month/year)
04.04.2003

International Patent Classification (IPC) or both national classification and IPC
A61K35/78

Applicant
INDENA S.P.A.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITYInternational application No.
PCT/EP2004/003055

10/551772

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/003055

Box No. II Pri rity

1. ☒ The following document has not been furnished:
- ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
 - ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).
- Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|--------|
| Novelty (N) | Yes: Claims | 1-7,10 |
| | No: Claims | 8,9 |
| Inventive step (IS) | Yes: Claims | 1-7 |
| | No: Claims | 8-10 |
| Industrial applicability (IA) | Yes: Claims | 1-10 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item V

1. The following documents are referred to in this communication:

D1 : CH 672 251 A

D2 : PHYTOCHEMISTRY, vol. 58, no. 5, November 2001, pages 763-767

D3 : JOURNAL OF NATURAL PRODUCTS, vol. 64, no. 3, March 2001, pages 399-400

D4 : GB 1 604 225 A

D5 : PATENT ABSTRACTS OF JAPAN vol. 2000, no. 24, 11 May 2001 (2001-05-11) &; JP 2001 206819 A

- 1.1 Document D1 discloses oestrogenic pharmaceutical compositions comprising ferutinine obtained by extraction from ferula plants.
- 1.2 Document D2 discloses the antibacterial activity of ferutinine and that ferula extracts have been used for the treatment of skin diseases in folk medicine.
- 1.3 Document D3 discloses the antibacterial activity of ferutinine isolated from *Ferula hermonis*.
- 1.4 Document D4 discloses the medical use of *Ferula Communis* extracts.
- 1.5 Document D5 discloses bleaching cosmetics made from plant extracts from amongst others *Ferula* species.

2. Novelty and Inventive Step:

- 2.1 Claim 1 relates to a process for the preparation of ferutinine by esterification with p-pivaloylbenzoic acid. The closest prior art is represented by the referenced prior art document J. Org. Chem. USSR (page 2) which differs in that other benzoic acids are employed. In the application a yield of 92,4 % is described compared to 45 % in the prior art. The problem to be solved can therefore be regarded as to provide better transesterification agents. As there is no indication in the prior art as to use p-pivaloylbenzoic acid, the subject-matter of claim 1 and dependent claims 2-7 seems to involve an inventive step.

- 2.2 In view of documents D1-D5 the subject-matter of claims 8 and 9, relating to the preparation of compositions comprising ferula extracts and ferutinine, respectively, is not new in the sense of Article 33(2) PCT.
- 2.3 Although none of the prior art documents disclose the use of p-pivaloyloxyferutinine for the preparation of compositions, the subject-matter of claim 10 does not seem to be inventive as there is no indication that the problem was solved.

Re Item VII

3. The structure of the formulae seem to be wrong in that in the position 8a a hydrogen atom is missing.